PA NT COOPERATION TREAT

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Commissioner
US Department of Commerce
United States Patent and Trademark Office, PCT
2011 South Clark Place Room CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 01 March 2001 (01.03.01)	
International application No. PCT/US00/15396	**Applicant's or agent's file reference** 00537-190WO1
International filing date (day/month/year) 05 June 2000 (05.06.00)	**Priority date** (day/month/year) 04 June 1999 (04.06.99)
Applicant SADAT-AALAEE, Dean et al	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

04 January 2001 (04.01.01)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland**	Authorized officer Antonia Muller
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

PCT US00/15396
JRG
4RT

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTICE INFORMING THE APPLICANT OF THE COMMUNICATION OF THE INTERNATIONAL APPLICATION TO THE DESIGNATED OFFICES

(PCT Rule 47.1(c), first sentence)

To:
TSAO, Rocky, Y.
Fish & Richardson P.C.
225 Franklin Street
Boston, MA 02110-2804
ETATS-UNIS D'AMERIQUE

CAB

Date of mailing (day/month/year) 14 December 2000 (14.12.00)	
Applicant's or agent's file reference 00537-190WO1	**IMPORTANT NOTICE**

International application No.	**International filing date** (day/month/year)	**Priority date** (day/month/year)
PCT/US00/15396	05 June 2000 (05.06.00)	04 June 1999 (04.06.99)

Applicant
BIOMEASURE INCORPORATED et al

1. Notice is hereby given that the International Bureau has communicated, as provided in Article 20, the international application to the following designated Offices on the date indicated above as the date of mailing of this Notice:
   AU,KP,KR,MZ,US

   In accordance with Rule 47.1(c), third sentence, those Offices will accept the present Notice as conclusive evidence that the communication of the international application has duly taken place on the date of mailing indicated above and no copy of the international application is required to be furnished by the applicant to the designated Office(s).

2. The following designated Offices have waived the requirement for such a communication at this time:
   AE,AL,AM,AP,AT,AZ,BA,BB,BG,BR,BY,CA,CH,CN,CR,CU,CZ,DE,DK,DM,EA,EE,EP,ES,FI,GB,GD,GE,GH,GM,HR,HU,ID,IL,IN,IS,JP,KE,KG,KZ,LC,LK,LR,LS,LT,LU,LV,MA,MD,MG,MK,MN,MW,MX,NO,NZ,OA,PL,PT,RO,RU,SD,SE,SG,SI,SK,SL,TJ,TM,TR,TT,TZ,UA,UG,UZ,VN,YU,ZA,ZW
   The communication will be made to those Offices only upon their request. Furthermore, those Offices do not require the applicant to furnish a copy of the international application (Rule 49.1(a-bis)).

3. Enclosed with this Notice is a copy of the international application as published by the International Bureau on
   14 December 2000 (14.12.00) under No. WO 00/75186

REMINDER REGARDING CHAPTER II (Article 31(2)(a) and Rule 54.2)

If the applicant wishes to postpone entry into the national phase until 30 months (or later in some Offices) from the priority date, a demand for international preliminary examination must be filed with the competent International Preliminary Examining Authority before the expiration of 19 months from the priority date.

It is the applicant's sole responsibility to monitor the 19-month time limit.

Note that only an applicant who is a national or resident of a PCT Contracting State which is bound by Chapter II has the right to file a demand for international preliminary examination.

REMINDER REGARDING ENTRY INTO THE NATIONAL PHASE (Article 22 or 39(1))

If the applicant wishes to proceed with the international application in the national phase, he must, within 20 months or 30 months, or later in some Offices, perform the acts referred to therein before each designated or elected Office.

For further important information on the time limits and acts to be performed for entering the national phase, see the Annex to Form PCT/IB/301 (Notification of Receipt of Record Copy) and Volume II of the PCT Applicant's Guide.

RECEIVED

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer J. Zahra
Facsimile No. (41-22) 740.14.35	Telephone No. (41-22) 338.83.38

DEC 26 2000
FISH & RICHARDSON
BOSTON OFFICE

Form PCT/IB/308 (July 1998)

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

by fax and post

PCT

To:

TSAO, Y. Rocky
FISH & RICHARDSON P.C.
225 Franklin Street
Boston, Massachusetts 02110-2804
ETATS-UNIS D'AMERIQUE

#001-617-542-8906

RECEIVED
SEP 21 2001
FISH & RICHARDSON, P.C.
BOSTON OFFICE

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Rule 71.1)

Date of mailing *(day/month/year)*	17.09.2001
Applicant's or agent's file reference 00537-190WO1	**IMPORTANT NOTIFICATION**

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US00/15396	05/06/2000	04/06/1999

Applicant
SOCIETE DE CONSEILS DE RECHERCHES ET.... et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

* No Docketing Required
Reviewed By Practice Systems
Initials:
Reviewed by Authorized Officer

Name and mailing address of the IPEA/

European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized officer

Neumann, M

Tel.+49 89 2399-7351

Form PCT/IPEA/416 (July 1992)

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
00537-190WO1		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US00/15396	05/06/2000	04/06/1999
International Patent Classification (IPC) or national classification and IPC C07K14/655		
Applicant SOCIETE DE CONSEILS DE RECHERCHES ET.... et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
04/01/2001	17.09.2001
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Kronester-Frei, A Telephone No. +49 89 2399 8555

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US00/15396

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:
Description, pages:

1-52 as originally filed

Claims, No.:

1-26 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 26.

because:

☒ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-26
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-26
Industrial applicability (IA)	Yes:	Claims	1-25

No: Claims 26

2. Citations and explanations
see separate sheet

VIII. *Certain observations on the international application*

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
se separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claim 26 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT). However the opinion given under Item V embraces the subject-matter being covered by those claims which might possibly redrafted in a subsequent European Examination Procedure.

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. The following documents (D) are referred to in this communication; the numbering corresponds to the order used in the Search Report, the numbering will be adhered to in the rest of the procedure:
   D1: WO-A-9405310
   D2: WO-A-9303056
   D3: EP-A-0478101
   D4: WO-A-9925729
   D5: WO-A-9851332
   D6: EP-A-0127899
   D7: Pept. 1996, Proc. Eur. Pept. Symp., 24th (1998), Meeting Date 1996, 483-484. Editor(s): Ramage, Robert;epton, Roger. Publisher: Mayflower Scientific, Kingswinford, Uk. (0000), , -
   D8: Pept. Proc. Am. Pept. Symp., 15th (1999), Meeting Date 1997, 526-529. Editor(s): Tam, James P.;kaumaya, Pravin T. P. Publisher: Kluwer, Dordrecht, Neth. (0000), , -
   D9: J. Pharmacol. Exp. Ther. (1999), 290(3), 1202-1211 (0000), , -
   D10: US-A-5462926

D1: Peptide inhibitors of cellular adhesion having the intrapeptidic bond bridging 2 amino acids.

D2 Improving of a biological activity of a peptide by a intrapeptidic S-S chain bridging 2 amino acids, better than the naturally occurring amino acids, lanthonin.

D3 Peptides having thrombospondin-like activity having a intrapeptidic s-s chain bridging 3 amino acids.

D4 Peptides having antitumour activity having an intrapeptidic S-S chain bridging 3 amino acids.

D5 Somatostatin and Somatostatin antagonists for treating insulin having cyclic peptidic ring structures.

D6 Cyclic peptapeptides displaying somatostatin antagonism.

D7: Test-System applied: Effector coupling of somatostatin receptor subtypes sst-1 and sst-2 as examined in a reconstituted system. Forskolin-stimulated cyclic adenosine monophosphate (cAMP) formation was inhibited 66% by somatostatin (SRIF-14) in CHO cells expressing somatostatin receptor 1 (sst-1) (CHO-SR1), but not sst-2, in a dose-dependent manner with an ED-50 of 1 times 10-9 mol/L SRIF-14.

D8, D9, D11: Different somatostatin analogs bridging 4 amino acids by a C-C-bond.

D10: Neuromedin B Receptor Antagonist

2. With respect to the documents cited in the Search Report novelty of the subject-matter claimed can be acknowledged.

3. As far as the requirements of inventive step of the Neuromedin B and somatostatin receptor antagonists claimed are concerned it would appear that a person skilled in this art confronted with the problem of looking for further Neuromedin B and somatostatin receptor antagonists being useful in the treatment of various diseases (cf. page 2, line 15ff) and functioning as potent mu opioid receptor antagonists would in principle have been able to further modify the different peptidic structures as cited in D1/D2, D3/D4 or in D5/D6. However the application of an affinity test for human somatostatin subtype receptors 1 to 5 (sst1, sst2, sst3, sst4, sst5), which is determined by measuring the inhibition of [125I-Tyr11]SRIF-14 binding to CHO-K1 cells transfected with the sst receptor

subtype, seems to require particular structural features in the Neuromedin B and somatostatin receptor antagonists claimed. This test is considered as representing an additional functional feature in the product claims, which information seem to be missing until now in the claims. This test enables to take a conclusion on structural requirements which cannot be deduced in an obvious manner from the teaching of the documents D1 to D6 vis-à-vis D7.
However, without such information it would appear that the skilled person confronted with the problem of looking for further Neuromedin B and somatostatin receptor antagonists being useful in the treatment of various diseases (cf. page 2, line 15ff) and functioning as potent mu opioid receptor antagonists would have been able to deduce in an obvious manner form the teaching of D1 to D6 that further modification in the bridging structure pattern of the peptides would result in peptides which show the same activity pattern as te peptides of the prior art D1 to D6. No inventive effort is required to further modify known peptides by applying different bridging structures of to build cyclic peptides. Therefore in the absence of such feature the requirements of inventive step of the product claims and dependent subject-matter are not satisfied.
It would appear that in a subsequent possible European application a deficiency of non-unity would be made.

4. For the assessment of the present claim 26 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Re Item VIII
Certain observations on the international application

The sentence on page 3, line 25/26 is considered to lead to unclear subject-matter (Article 6 PCT).

PATENT COOPERATION TREATY

RECD 19 SEP 2001
WIPO PCT

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

14

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
00537-190WO1		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US00/15396	05/06/2000	04/06/1999
International Patent Classification (IPC) or national classification and IPC C07K14/655		
Applicant SOCIETE DE CONSEILS DE RECHERCHES ET.... et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
04/01/2001	17.09.2001
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Kronester-Frei, A Telephone No. +49 89 2399 8555

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US00/15396

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:
Description, pages:

1-52 as originally filed

Claims, No.:

1-26 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 26.

because:

☒ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-26
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-26
Industrial applicability (IA)	Yes:	Claims	1-25

No: Claims 26

2. Citations and explanations
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claim 26 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT). However the opinion given under Item V embraces the subject-matter being covered by those claims which might possibly redrafted in a subsequent European Examination Procedure.

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. The following documents (D) are referred to in this communication; the numbering corresponds to the order used in the Search Report, the numbering will be adhered to in the rest of the procedure:
   D1: WO-A-9405310
   D2: WO-A-9303056
   D3: EP-A-0478101
   D4: WO-A-9925729
   D5: WO-A-9851332
   D6: EP-A-0127899
   D7: Pept. 1996, Proc. Eur. Pept. Symp., 24th (1998), Meeting Date 1996, 483-484. Editor(s): Ramage, Robert;epton, Roger. Publisher: Mayflower Scientific, Kingswinford, Uk. (0000), , -
   D8: Pept. Proc. Am. Pept. Symp., 15th (1999), Meeting Date 1997, 526-529. Editor(s): Tam, James P.;kaumaya, Pravin T. P. Publisher: Kluwer, Dordrecht, Neth. (0000), , -
   D9: J. Pharmacol. Exp. Ther. (1999), 290(3), 1202-1211 (0000), , -
   D10: US-A-5462926

D1: Peptide inhibitors of cellular adhesion having the intrapeptidic bond bridging 2 amino acids.

D2 Improving of a biological activity of a peptide by a intrapeptidic S-S chain bridging 2 amino acids, better than the naturally occurring amino acids, lanthonin.

D3 Peptides having thrombospondin-like activity having a intrapeptidic s-s chain bridging 3 amino acids.

D4 Peptides having antitumour activity having an intrapeptidic S-S chain bridging 3 amino acids.

D5 Somatostatin and Somatostatin antagonists for treating insulin having cyclic peptidic ring structures.

D6 Cyclic peptapeptides displaying somatostatin antagonism.

D7: Test-System applied: Effector coupling of somatostatin receptor subtypes sst-1 and sst-2 as examined in a reconstituted system. Forskolin-stimulated cyclic adenosine monophosphate (cAMP) formation was inhibited 66% by somatostatin (SRIF-14) in CHO cells expressing somatostatin receptor 1 (sst-1) (CHO-SR1), but not sst-2, in a dose-dependent manner with an ED-50 of 1 times 10-9 mol/L SRIF-14.

D8, D9, D11: Different somatostatin analogs bridging 4 amino acids by a C-C-bond.

D10: Neuromedin B Receptor Antagonist

2. With respect to the documents cited in the Search Report novelty of the subject-matter claimed can be acknowledged.

3. As far as the requirements of inventive step of the Neuromedin B and somatostatin receptor antagonists claimed are concerned it would appear that a person skilled in this art confronted with the problem of looking for further Neuromedin B and somatostatin receptor antagonists being useful in the treatment of various diseases (cf. page 2, line 15ff) and functioning as potent mu opioid receptor antagonists would in principle have been able to further modify the different peptidic structures as cited in D1/D2, D3/D4 or in D5/D6. However the application of an affinity test for human somatostatin subtype receptors 1 to 5 (sst1, sst2, sst3, sst4, sst5), which is determined by measuring the inhibition of [125I-Tyr11]SRIF-14 binding to CHO-K1 cells transfected with the sst receptor

subtype, seems to require particular structural features in the Neuromedin B and somatostatin receptor antagonists claimed. This test is considered as representing an additional functional feature in the product claims, which information seem to be missing until now in the claims. This test enables to take a conclusion on structural requirements which cannot be deduced in an obvious manner from the teaching of the documents D1 to D6 vis-à-vis D7.
However, without such information it would appear that the skilled person confronted with the problem of looking for further Neuromedin B and somatostatin receptor antagonists being useful in the treatment of various diseases (cf. page 2, line 15ff) and functioning as potent mu opioid receptor antagonists would have been able to deduce in an obvious manner form the teaching of D1 to D6 that further modification in the bridging structure pattern of the peptides would result in peptides which show the same activity pattern as te peptides of the prior art D1 to D6. No inventive effort is required to further modify known peptides by applying different bridging structures of to build cyclic peptides. Therefore in the absence of such feature the requirements of inventive step of the product claims and dependent subject-matter are not satisfied.
It would appear that in a subsequent possible European application a deficiency of non-unity would be made.

4. For the assessment of the present claim 26 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Re Item VIII
Certain observations on the international application

The sentence on page 3, line 25/26 is considered to lead to unclear subject-matter (Article 6 PCT).